

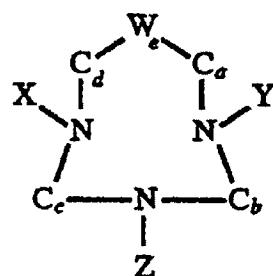
Amendments to the Claims:

The listing of claims will replace all prior versions and listings of claims in the application:

Listing of the Claims

1.-28. Canceled

29. (Currently amended) A method for treating an individual suffering from a pathological conditions which is ~~ameliorated~~ ameliorated by ~~supression~~ suppression of CD4+-T-cell-mediated immune response, other than a condition resulting from viral infection, which comprises the ~~steps~~ step of administering to the individual a therapeutically effective amount or combined amount of one or more triaza macrocyclic compounds having the formula:



or a pharmaceutically acceptable salt or solvate thereof, that is effective for downregulating expression of CD4,

wherein:

W represents a bridge carbon which is unsubstituted or which is bonded directly or indirectly to one or two polar or non-polar side group substituents selected from the group of double-bonded carbon (=C(H)₂ or =C(R)₂), double bonded oxygen (=O), hydroxyl, alkyl of one to 10 carbons, alkenyl of two to 10 carbons, a substituted alkyl group carrying a charged substituent, alkoxy of one to 10

carbons, aryl of 6 to 12 carbons, halogen, methyl halogen, methylene halide, optionally substituted epoxide, $-\text{COR}$ group, $-\text{CO}_2\text{R}$, CH_2OH or hydrogen; where R, independently of other R, is an optionally substituted alkyl of one to 10 carbons, an optionally substituted alkenyl group of about 2 to 10 carbon atoms or an optionally substituted aryl group of about 6 to 12 carbons and W may be bonded to one hydrogen and one polar or non-polar group;

X and Y, independently, represent an optionally substituted aryl (Ar), an optionally substituted alkyl having from one to 10 carbon atoms, or an optionally substituted alkenyl having from 2 to 10 carbon atoms attached to the triaza macrocycle through an optional linker group L, where the linker group L is selected from sulfonyl ($-\text{SO}_2-$), $-\text{SO}-$, $-\text{PO}-$, $-\text{PO(OH)}-$, $-\text{PO(H)}-$, $-\text{PO}_2(\text{OH})-$, $-\text{PO}_2(\text{H})-$, $-\text{PO}_3(\text{OH})-$, carboxy ($-\text{OCO}-$), carbonyl ($-\text{CO}-$), or alkyl, where Ar comprises at least one aromatic homocyclic or heterocyclic ring having from five to seven members and wherein X and Y are not both alkyl groups;

Z represents a hydrogen, or optionally substituted aryl, alkyl or alkenyl groups attached to the triaza macrocycle through optional linking group L^3 , wherein the aryl, alkyl and alkenyl groups are as defined for X and Y variables above and L^3 is as defined for L above;

~~Optional substitution includes substitution with one or more non-hydrogen substituent groups selected from halogens, CN , SO_3 , SH , SR , S-OR , trihalomethyl, NO , NO_2 , NH_2 , NHR , $\text{N}(\text{R})_2$ alkyl, alkoxy, hydroxyl, COH , CO-R , CO_2H or CO_2R groups, where R, independently of other R is an alkyl of one to 10 carbons or an aryl group of 6 to 12 carbons;~~

wherein optionally substitution is substitution by one or more charged, polar or non-polar groups:

where charged substituents are selected from the group consisting of an

$\text{-S}(\text{R}'')_2^+$, an $\text{-N}(\text{R}'')_3^+$, a -PR''_3^+ , and an -OSO_3^- group, where R'' is independent of other R'' , a hydrogen or an alkyl group having from one to 10 carbon atoms;

where polar substituents are selected from the group consisting of halogen, -CT_3 , -NH_2 , $\text{-N}(\text{R}')_2$, -NO , -NO_2 , -SH , $\text{-SO}_3\text{H}$, $\text{SO}_3\text{R}'$, -OH , -COH , $\text{-COR}'$, -CONH- , $\text{-CONR}'$, $\text{-CO}_2\text{H}$ and $\text{-CO}_2\text{R}'$, where each T independently is a halogen, and where each R' independently is alkyl or alkenyl having one to 10 carbon atoms and aryl, and

where non-polar substituents are selected from the group consisting of alkyl groups, alkenyl groups, unsubstituted aryl groups, $\text{-OR}'$, $\text{-(CH}_2\text{)}_n\text{-OR}'$, $\text{-SR}'$, $\text{-(CH}_2\text{)}_n\text{-SR}'$, where n is an integer that is 1 or more and where each R' independently is alkyl or alkenyl having one to 10 carbon atoms and aryl, and

where alkyl, alkenyl or aryl groups of these substituents can themselves be substituted with one or more polar or non-polar groups; and

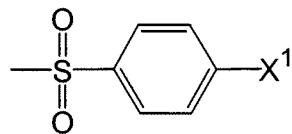
wherein optional substituents of Ar groups can further be selected from the group consisting of one or more halogens, one or more -CN ; one or more $\text{-SO}_3\text{H}$, -SH , -SR_{Ar} , or -S-OR groups; one or more trihalomethyl groups; one or more -NO , one or more -NO_2 , one or more -NH_2 , -NHR_{Ar} or $\text{N}(\text{R}_{\text{Ar}})_2$ groups; one or more alkyl groups; one or more alkoxy groups; one or more hydroxyl groups; one or more acyl groups; one or more acid or ester groups; where R_{Ar} , independently of other R_{Ar} , is an alky of about one to 10 carbons or an aryl group of about 7 to 10 carbons;

C labeled with subscripts a-d C_a , C_b , C_d , and C_e , represent carbon bridges between nitrogens, the length of which is are defined by the values of subscripts a-d and e, the carbon bridges may all be the same length or may differ in length, and each carbon bridge may be composed entirely of saturated alkyl groups, or

one or more bridges may contain one or more double or triple bonds between carbons, one or more bridge carbons are optionally substituted with one or more polar groups and aromatic, non-aromatic rings or both are optionally fused to one or more of the carbon atom bridges; and

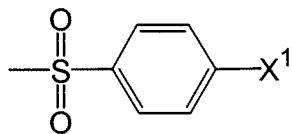
a and d, independently, represent a number from zero to 10; b and c, independently, represent a number from one to 10; and e represents a number from zero to three and a + d + e ≥ 1.

30. (Currently amended) The method of claim 29 wherein e is 1 and W is double-bonded carbon (=C(H)₂ or =C(R)₂), a double bonded oxygen (=O), or a methylene halide,
where R independently of other R, is an optionally substituted ~~alky alkyl~~ of about one to 10 carbons, an optionally substituted alkenyl group of about 2 to 10 carbon atoms or an optionally substituted aryl group of about 6 to 12 carbons.
31. (Previously presented) The method of claim 29 wherein X and Y, independently, are optionally substituted aryl groups attached to the triaza macrocycle through an optional linker group L selected from –SO₂ –, –SO–, –PO –, –PO(OH) –, –PO(H) –, –PO₂(OH)–, –PO₂(H) –, –PO₃(OH) –, -OCO-, -CO-, or alkyl.
32. (Previously presented) The method of claim 31 wherein L is –SO₂ –.
33. (Previously presented) The method of 32 wherein X and Y are selected from tosyl groups, dansyl groups or analogues thereof.
34. (Previously presented) The method of claim 29 wherein X and Y groups have the structure:



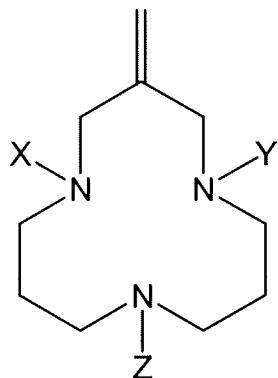
where X¹ is a group selected from a halogen, -CN, -SO₃, -SH, -SR, -S-OR, trihalomethyl, -NO, -NO₂, -NH₂, -NHR, -N(R)₂, alkyl, alkoxy, hydroxyl, -COH, -COR, -CO₂H, or -CO₂R.

35. (Previously presented) The method of claim 29 wherein Z is an optionally substituted aryl, alkyl or alkenyl group optionally attached to the triaza macrocycle though a linking group L³ selected from -SO₂ -, -SO-, -PO -, -PO(OH) -, -PO(H) -, -PO₂(OH)-, -PO₂(H) -, -PO₃(OH) -, -OCO-, -CO-, or alkyl.
36. (Previously presented) The method of claim 29 wherein Z is an optionally substituted aryl, alkyl or alkenyl group directly attached to the triaza macrocycle.
37. (Previously presented) The method of claim 29 wherein Z is a benzyl group.
38. (Previously presented) The method of claim 29 wherein Z is a benzyl group, a methylene cyclohexane group or a methylene cyclohexene group.
39. (Previously presented) The method of claim 29 wherein a, d and e are all 1 and b and c are 3.
40. (Previously presented) The method of claim 29 wherein e is 1 and W is >C=C(H)₂.
41. (Previously presented) The method of claim 29 wherein X and Y have the structure:



wherein X¹ is a group selected from a halogen, -CN, -SO₃, -SH, -SR, -S-OR, trihalomethyl, -NO, -NO₂, -NH₂, -NHR, -N(R)₂, alkyl, alkoxy, hydroxyl, -COH, -COR, -CO₂H, or -CO₂R.

42. (Previously presented) The method of claim 41 wherein X¹ is an alkyl, alkoxy or hydroxyl group.
43. (Previously presented) The method of claim 29 wherein the one or more triaza macrocyclic compounds have the formula:



wherein X, Y and Z, independently, are optionally substituted aryl groups, optionally substituted alkyl groups having from one to 10 carbon atoms, or optionally substituted alkenyl groups having from 2 to 10 carbon atoms attached to the triaza macrocycle through an optional linker group L selected from -SO₂-, -SO-, -PO-, -PO(OH)-, -PO(H)-, -PO₂(OH)-, -PO₂(H)-, -PO₃(OH)-, carboxy (-OCO-), carbonyl (-CO-), or (CH₂)_n, where n is 1 or 2, and wherein X and Y are not both an alkyl group.

44. (Previously presented) The method of claim 43 wherein Z is a benzyl group directly bonded to N.

45. (Previously presented) The method of claim 43 wherein X and Y are both optionally substituted aryl groups linked to the triaza macrocycle through linker group L which is selected from $-\text{SO}_2-$, $-\text{SO}-$, $-\text{PO}-$, $-\text{PO(OH)}-$, $-\text{PO(H)}-$, $-\text{PO}_2(\text{OH})-$, $-\text{PO}_2(\text{H})-$, $-\text{PO}_3(\text{OH})-$, carboxy (-OCO-), carbonyl (-CO-), or $(\text{CH}_2)_n$, where n is 1 or 2.
46. (Previously presented) The method of claim 43 wherein X and Y are both optionally substituted aryl groups linked to the triaza macrocycle through linker group $-\text{SO}_2$.
47. (Previously presented) The method of claim 43 wherein X and Y are both optionally substituted phenyl groups linked to the triaza macrocycle through linker group $-\text{SO}_2-$.
48. (Previously presented) The method of claim 43 wherein X and Y are phenyl groups substituted with one or more alkyl groups, alkoxy groups, $-\text{NO}_2$ groups, $-\text{NH}_2$ groups, or halides.
49. (Previously presented) The method of claim 48 wherein X and Y are para-substituted phenyl groups.
50. (Previously presented) The method of claim 48 wherein X and Y are para-substituted phenyl groups wherein the para-substituents are alkyl groups or alkoxy groups.
51. (Previously presented) The method of claim 43 wherein X and Y are optionally substituted phenyl groups optionally linked to the linked to the triaza macrocycle through linker group L which is selected from $-\text{SO}_2-$, $-\text{SO}-$, $-\text{PO}-$, $-\text{PO(OH)}-$,

–PO(H) –, –PO₂(OH)–, –PO₂(H) –, –PO₃(OH) –, carboxy (–OCO–), carbonyl (–CO–), or (CH₂)_n, where n is 1 or 2.

52. (Previously presented) The method of claim 51 wherein Z is an optionally substituted phenyl group optionally linked to the linked to the triaza macrocycle through linker group L which is selected from –SO₂ –, –SO–, –PO –, –PO(OH) –, –PO(H) –, –PO₂(OH)–, –PO₂(H) –, –PO₃(OH) –, carboxy (–OCO–), carbonyl (–CO–), or (CH₂)_n, where n is 1 or 2.
53. (Previously presented) The method of claim 52 wherein X and Y are optionally substituted phenyl groups linked to the linked to the triaza macrocycle through –SO₂ –.
54. (Previously presented) The method of claim 53 wherein Z is a benzyl group.
55. (Previously presented) The method of claim 54 wherein X and Y are para-substituted phenyl groups.
56. (Previously presented) The method of claim 55 wherein X and Y are para-substituted phenyl groups wherein the para-substituent is an alkoxy group or an alkyl group.
57. (Previously presented) The method of claim 55 wherein the para-substituent is a methoxy group or a methyl group.
58. (Previously presented) The method of claim 29 wherein the pathological condition is an autoimmune disorder or a chronic inflammatory disease.
59. (Previously presented) The method of claim 29 wherein the pathological condition is graft-versus host disease or transplant rejection.

60. (Currently amended) The method of claim 29 wherein the pathologic condition is rheumatoid arthritis, type I-diabetes mellitus, autoimmune demyelinating diseases, ~~such as~~ multiple sclerosis, inflammatory bowel disease syndrome, psoriasis, discoid lupus erythematosus, systemic lupus erythematosus (SLE), adult respiratory distress syndrome, cardiovascular atherosclerosis, leukocytosis, or asthma.
61. (New) The method of claim 29 wherein e is 1, a and d are 1 to 3, and b and c are 2-4.
62. (New) The method of claim 29 wherein a, d and e are all 1.
63. (New) The method of claim 29 wherein the pathologic condition is an autoimmune disorder.